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Does Tiron offer cardio protection from myocardial injury induced Doxorubicin?

Background: The heart is a frequent site of drug adverse effects resulting in structural changes through damage to cardiomyocytes, and associated myocardial injury (1). These injuries may be a result of direct toxic effects of the drugs or on the metabolic pathways, leading to enhanced production of reactive oxygen species. Doxorubicin, an effective anticancer drug, has been demonstrated to induce cardiac toxicity through the formation of free radicals (2, 3). Several studies have revealed that the intake of antioxidants decreases the damaging effect of free radicals (ROS) (4,5). Recently, investigations carried out with the antioxidant Tiron, demonstrated a high degree of protection against ROS related injury in skin cells (6).

Aims and objectives: The study undertaken aimed to investigate the role of Tironas a protective adjunctive agent against doxorubicin induced myocardial injury.

Methods: *The* Langendorff perfused rat heart model was used to assess the effects of Tiron as a protective adjunctive agent against doxorubicin induced myocardial injuryby ligation(3). Tiron (0.25mM, 0.5mM and 1mM) was assessed in the Langendorff heart model (n=6-8) alone and in the presence of Doxorubicin (1µM). Hearts underwent triphenyltetrazolium chloride staining for the assessment of the infarct ratios. *MTT* (*3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assays were performed with* HepG2 liver carcinoma cells to assess the efficacy of Doxorubicin (1µM) on cell viability in combination with Tiron (0.25mM-2.5mM) (7). Data arepresented as the mean +/-SEM and analysed by one-way ANOVA and Fischer's LSD post test. Significance is considered P value ≤0.05

Results: A significant reduction in infarct size to risk ratio was observed when hearts were treated with Doxorubicin and Tiron 0.25mM (14.79±0.67%) and 0.5mM (15.59±0.58%) compared to Doxorubicin treatment alone (31.27±2.55%). In HepG2 no significant decrease in doxorubicin induced cell toxicity was seen with the inclusion of Tiron in culture.

Conclusions: This study shows that the antioxidant Tiron is able to reduce the myocardial injury induced by Doxorubicin. This study indicates no reduction in the efficiacy of Doxorubicin in HepG2 cells in the presence of Tiron. Further studies are required to assess the efficacy in other cell lines such as HL60 leukaemia cells. These data support the potential use of Tiron as an adjunctive agent to prevent off targets cardiotoxicity seen with Doxorubicin treatment.

References:

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